The Examiner asserted that certain aspects of the claims are broader than the enabling disclosure provided in the specification. Particularly, with respect to combinations of pyridinium compound(s) and nicotinic and/or muscarinic and/or glutamate antagonists, the Examiner asserted that there is not seen sufficient representation in the instant specification wherein a 3-substituted pyridinium compound is combined with nicotinic, muscarinic and glutamate antagonists as one composition, nor wherein the 3-substituted pyridinium compound is combined with a lone antagonist. Thus, the Examiner asserted that without adequate representation to establish dosage and effective concentrations of the pyridinium compound and the antagonist, one of skill in the art would be faced with undue experimentation in the practice of the instantly claimed composition.

In response, Applicants traverse the Examiner's rejection of claim 14 under 35 U.S.C. §112, first paragraph. Applicants contend that the specification provides enablement for the scope of claim 14. Specifically, on pages 24-26, applicants discuss the role of pyridinium derivative PO in reversal of scopolamine-induced cognitive impairment in rats (page 24-26). Scopolamine is a centrally active antimuscarinic drug that induces a profound decrement in learning and memory. Anticholinersterases can reverse this impairment, provided they are accessible to the CNS. Applicants show that PO is able to reverse scopolamine-induced impairment of acquisition in passive avoidance behavioral task, at a dose of 15 mg and 25 mg/kg PO and 0.3 mg/kg scopolamine. Thus the subject application supports a combination of a pyridinium compound and an antimuscarinic drug, including establishment of dosage and effective concentrations of the pyridinium compound and the antagonist, in such a way as to enable one skilled in the art to make or use the invention. Applicants contend that in view of the above-mentioned example, it would have been obvious to use nicotinic and/or muscarinic and/or glutamate antagonists in combination with the 3-positioned pyridinium compounds for the treatment of hypercholinergic impairments. Nicotinic receptors and muscarinic receptors are subtypes of the cholinergic receptors. It is well known in the art and can be supported by toxicological literature (McDonough et al, *Pharmacol. Biochem. Behav.* 1995, 51, 249-53; McDonough et al, *Neurosci. Biobehav. Rev.* 1993, 17, 203-15; and Lallement G et al, 1992, *Neurosci. Lett.*, 139, 104-7),that the sequella of acetylcholine poisoning include the cholinergic receptors and the glutamate receptor complex.

Thus, Applicants maintain that adequate representation exists in the Specification for the pyridinium compound in combination with any of nicotinic and/or muscarininc and/or glutamate receptor antagonists.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection under 35 U.S.C. §112, first paragraph.

Rejections under 35 U.S.C. §112, Second Paragraph

In the Office Action, the Examiner rejected Claims 1-14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants submit that claims 1-14 have been cancelled without prejudice or disclaimer, and that the new claims 15-40 have been added which are in compliance with requirement under 35 U.S.C. 112, second paragraph. Accordingly, Applicants respectfully request withdrawal of the rejections.

Rejections under 35 U.S.C. §103

In the Office Action, the Examiner rejected claims 1-13 under 35 U.S.C. §103 as being unpatentable over Bodor, U.S. Patent No. 4,824,850 and Naito, JP 05339148 A2 (abstract). The Examiner asserted that Bodor teaches the use of pyridinium derivatives and associated salts for the delivery of pharmaceuticals through the blood brain barrier (BBB). The Examiner further asserted that Naito teaches the use of sugars to allow pharmaceuticals to pass through the blood brain barrier. The Examiner alleged that it would have been obvious to modify the teachings of Bodor in view of Naito to obtain the claimed invention.

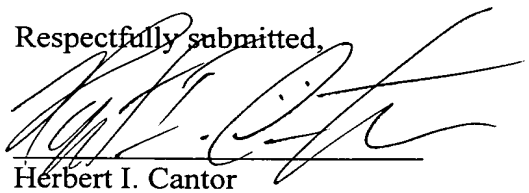
In response, Applicants traverse the Examiner's rejection of claim 1-13 under 35 U.S.C. §103. Contrary to the Examiner's statements, Bodor uses neutral reduced compounds to enter the brain, which are oxidized inside the brain to yield charged compounds, while the subject matter of claims 1-13 is directed to charged pyridinium derivatives which enter the brain by virtue of a lipophillic moiety attached to them and a sugar moiety that enhances their transport. Thus Bodor's teachings are irrelevant to the present invention

Furthermore, the knowledge of increasing bioavailablity by introducing certain sugars into the molecule is indeed a common knowledge. However, the subject matter of claims 1-13 is not related to the "concept" which is known in the art, but rather to the novel and nonobvious molecular entity, which comprises a charged moiety linked to a sugar and which required experimentation to develop.

Since the Examiner's objection in view of Bodor and Naito has been overcome, the combination of both citations is also mute. Accordingly, applicants respectfully rquest the Examiner to reconsider and withdraw the rejection under 35 U.S.C. §103.

Applicants believe that they have addressed all issues raised by the Examiner and that the claims as amended are in condition for allowance, which is earnestly requested. If the Examiner wishes to discuss any aspect of this response, or any suggestions and extant issues, he is encouraged to telephone the undersigned. No additional fee in required.

Respectfully submitted,



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